PROGNOSTIC FACTOR FOR SURVIVAL OF LUNG CANCER PATIENT IN DR.WAHIDIN SUDIROHUSODO HOSPITAL MAKASSAR

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Abstract

Lung cancer is not only the most common cause of death from cancer worldwide but also highest new cases of cancer in both men and women. It is estimated that there are 1.8 million new cases in 2012 (12.9% of the total), 58% of them occur in less developed regions. This research aimed to found out the proportion of the determinant of survival in lung cancer patients who came for treatment in Makassar during the period of 2012-2016 based on prognostic factors. The study was conducted at Dr. Wahidin Sudirohusodo Hospital, Makassar using observational analytic with Retrospective Cohort Study design. The samples were choosen using the exhaustive sampling method, and the total sample was 144 patients diagnosed with lung cancer and recorded in the medical records of DR Wahidin Sudirohusodo Hospital during the period of 2012-2016. Data were analyzed using the Kaplan-Meier curves, log rank test and cox regression. The results showed that The proportion of lung cancer survival with a BMI <18,5 was 6% and BMI ≥ 18,5 was 50% with HR 3,163 (95% CI = 1,802 – 5,551); severe comorbidities was 7% and mild comorbidity was 20% with HR 1,599 (95% CI = 1,110 – 2,302); bad performance status was 11% and good performance status was 21% with HR 1,987 (95% CI = 1,335 – 2,960). The study concluded that the BMI, comorbidity and performance status are prognostic factors that affect the survival of lung cancer patients.

Keywords: Lung cancer, survival, prognosis

INTRODUCTION

Lung cancer is not only the most common cause of cancer deaths worldwide but also the disease with the highest new cases in both men and women.[1] An estimated 1.8 million new cases in 2012 (12.9% of total), 58% of them occur in less developed areas. The incidence of lung cancer in Southeast Asia was 29.6 per 100,000 in men and 11.9 per 100,000 in women.[2]

Based on the data of Cancer Country Profiles 2014, the incidence of lung cancer in Indonesia in 2014 amounted to 34 696 cases, 25.322 cases in men and 9.374 in women. Number of cancer deaths in Indonesia in 2014 reached 195 300 deaths, of which 21.8% in men and 9.1% in women. .[3]

Although there have been some improvements in surgical and therapeutic techniques combined over the last few decades, the prognosis of lung cancer patients is still low. Globally the average survival is only 1 year and the 5-year survival rate is only about 16%. Life expectancy for five years after diagnosis ranged from 1% to 49%.[4] In the United States, 5-year survival for lung cancer by 17%.[5] In Europe, the 5-year survival rate is generally the same as that of the United States, as in Belgium the survival of lung cancer is 16.5%. Asian countries like China have a 5% survival rate of lung cancer patients of 21%, and in South Korea at 20%. While in India and Thailand the average 5-year survival rate of lung cancer is only 9%.[6] In Indonesia, 1-year survival rate of lung cancer by 13%, of which more than 60%.[7] And most patients who seek treatment have to be at an advanced stage (IIIB-IV).[8]

The nutritional status of patients with malignancy can affect the course of the disease, the effects of treatment, quality of life and sustainability of life of patients so that knowledge of the nutritional status in patients with malignancy is very important.[9] Research conducted in Canada in 2013, showed significant results that low weight was associated with low survival with HR values of 1.33 (95% CI 1.01-1.77, p = 0.045).[10] Similarly, the research results of Imai in 2015, which stated that low weight (<18.5) affects overall survival with HR = 1.54.[11]

Lung cancer is still a health problem that is difficult to overcome in Indonesia, due to the high mortality and morbidity of patients. Increased lung cancer patients also leads to higher death rates due to cancer, especially because patients come to treatment already at an advanced stage, so the handling is getting harder and the cure rate is getting smaller.[12] Cases of lung cancer based on the medical record RSUP Wahidin Sudirohusodo showed a considerable number of events. In 2014 the incidence of lung cancer recorded 194 cases. This study aims to determine the proportion of determinants of survival of patients with lung

cancer who treated in RSUP DR Wahidin Sudirohusodo Makassar period 2012-2016 based on prognostic factors.

MATERIALS AND METHODS

The study was conducted at Dr. Wahidin Sudirohusodo Hospital, Makassar using observational analytic with Retrospective Cohort Study design. The samples were choosen using the exhaustive sampling method, and the total sample was 144 patients diagnosed with lung cancer and recorded in the medical records of DR Wahidin Sudirohusodo Hospital during the period of 2012-2016.

Secondary data was obtained from tracing medical record data of lung cancer patients in Dr. Wahidin Sudirohusodo hospital. Primary data obtained by follow up by telephone to ask patient's survival status (event/sensor). Data analysis was performed with SPSS program and statistical test by using bivariate test and survival analysis using Kaplan-meier method and log-rank test followed by cox regression test to obtain Hazard Ratio value.

RESULTS

Age of respondents in this study quite varied with a range between 21-87 years. In this study, the highest age group was found in the age group of 47-55 years and 56-64 years, 44 persons or 30.6%, with deaths of 37 people (84.1%). Based on medical record data, lung cancer patients were 108 men, 81.5% of whom died at the end of the observation, and 36 women and 80.6% of them died from lung cancer (Table 1).

The proportion of cumulative survival of lung cancer patients 1-year was 24%, for 2-years survival 16%, and in the third year survival of lung cancer patients only 14%. The median value is 5,000. This means that 50% of lung cancer patients have died in the fifth month (figure 1).

Lung cancer deaths in patients with BMI <18.5 were 103 people (88.0%), while patients with BMI <18.5 survived by 11 people (40.7%). The HR score for IMT variables was 3.163 (95% CI 1.802-5.551), which means lung cancer patients with BMI <18.5 had risk 3.163 times greater for death than patients with BMI ≥ 18.5 (Table 2).

With log rank test obtained p value of 0.000 <0,05 so it is concluded that there is relation between BMI and lung cancer survival. From the curve of the Kaplan meier to the IMT we can see that there is no intersection on both curves then the proportional hazard assumption is fulfilled. It can be concluded that there are differences in survival of lung

cancer based on BMI. The difference in the proportion of survival was 6.6% for patients with BMI <18.5 and 50.4% for patients with BMI ≥ 18.5 (Figure 2).

Berdasarkan analisa tabulasi silang yang dilakukan diketahui bahwa pasien dengan komorbiditas berat yang mengalami kematian akibat kanker paru sebesar 47,9%, sedangkan pada pasien yang bertahan hidup hanya berjumlah 5 orang (18,5%), Nilai HR sebesar 1,599 dengan (CI 1,110 – 2,302) sehingga dapat disimpulkan bahwa pasien kanker paru dengan komorbiditas berat memiliki risiko meninggal akibat kanker paru sebesar 1,599 kali lebih besar dibandingkan pasien dengan komorbiditas ringan (Tabel 2).

The result of log rank test related to the correlation between comorbidity and survival of lung cancer patients showed significant result with p value = 0.007. While the Kaplan meier curve shows that the survival curve of lung cancer patients based on comorbidity does not intersect each other. This means that the probability of death from lung cancer by comorbidity meet the assumption of proportional hazards. The result of analysis with log rank test showed that p value less than 0.05 so it can be concluded that there is correlation between survival of lung cancer patient with patient comorbidity. The proportion of survival of lung cancer patients with severe comorbidities was 7%, and patients with mild comorbidities of 20% (figure 3).

The results of cross-tabulation analysis also showed that lung cancer deaths with poor performance status (karnofsky score <70) are 70% whereas in patients who survived, the percentage of patients with poor performance status was 40.7%. The HR score are 1,987 (CI 1,335 - 2,960), meaning that lung cancer patients with poor performance status significantly had a 1.987 times greater risk of death (Table 2).

The patient's survival curve based on performance status indicates that the curve does not intersect each other. This means that the probability of survival of lung cancer patients based on performance status meets the proportional hazard assumptions. The result of log rank test analysis showed less than 0.05 result so it was concluded that there was difference of event occurrence based on performance status. The proportion of survival of lung cancer patients with poor performance status was 11%, and performance status was good at 21% (figure 4).

DISCUSSION

This study shows the one-year survival rate in getting different from the results of research conducted by Supartono & Suryanto in 2012 in Semarang City with survival rate

18.29%.[16] Differences in survival rates were also obtained between the results of this study and the results of research by Rasyid et al in Jakarta in 2004, where the 2-year survival rate was 14%.[17] The increase in survival rates can be due to differences in treatment, as well as new findings or innovations in lung cancer treatment in recent years.

However, when compared with other countries such as developed countries like England, the 1-year survival rate in this study is still lower than in the UK where the 1-year survival rate is 32%.[18] In the United States, the 5-year survival rate is 16% higher than the 3-year survival rate in this study.[6] This difference is due to differences in technological progress in terms of handling and screening and early detection in developed countries compared to developing countries such as Indonesia. In addition, some patients diagnosed with lung cancer did not perform treatment according to medical planning such as rejecting chemotherapy, surgery, even refusing treatment, leading to lower proportion of survival.

Factors related to survival of lung cancer patients in this study were BMI, clinical stage, and type of treatment. IMT variable in this study is only categorized into 2 that is <18,5 and ≥ 18,5. The reason for categorization is only 2 groups and does not make the category for overweight and obesity because as well as good nutritional status, overweight and obesity according to previous theories and studies are protective against the survival of patients with lung cancer.[19]

In this study found that IMT significantly affect the survival of lung cancer patients. The results of this study are in line with previous studies conducted by Matsunaga et al 2015, which states that low BMI (<18.5) is a risk factor for lung cancer death (HR 4.86; CI 1,38-17,12).[20] Similar to the results of Luo et al's 2012 study, finding a low BMI (<18.5) was a significant prognostic factor for low survival (HR = 2.15).[21]

The importance of researching BMI due to some nutritional disorders is a result of the side effects of therapy used are often experienced by cancer patients. Determination of early stage nutrition status is very important, because at least 50% of cancer patients will experience weight loss and changes in nutritional status at the time of diagnosis.[22] The nutritional status of patients suffering from malignancy can affect the course of the disease, the effects of treatment, the quality of life and survival of patients. Therefore, knowledge of utritional status of malignant patients is important.[9] In every hospital needs a nutritionist who always control the patient's BMI and food coverage.

Patients with advanced lung cancer require special attention because often there has been a decline in kidney function, heart, liver, and have many other comorbid diseases that

need attention in giving therapy, especially systemic.[12] Comorbidity is a disease that affects the patient's condition, but not as a result of the cancer experienced. The presence of comorbidities will affect the survival of patients. Lung cancer patients who are comorbid with other diseases such as chronic obstructive pulmonary disease, diabetes, and congestive heart failure have a 30% higher risk of dying from lung cancer.[23]

The comorbidity rate in lung cancer patients was assessed using the CCI method of categorizing patient comorbidities under the International Classification of Diseases (ICD) code, where each category of comorbidity was weighted based on the risk of death. The higher the comorbidity score the greater the probability the predicted result will lead to death. Assessment of comorbidities in this study were grouped into 2 groups, mild comorbidities with comorbidity score <2 and severe comorbidities with score ≥2, where the scoring was based on the charlson comorbidity index.

The results showed that 61 people suffering from severe comorbidities only 5 survived until the end of the observation. Other diseases most commonly found in lung cancer patients are respiratory diseases such as COPD, pneumonia, TB, pleural effusion. In addition, many lung cancer patients who have metasase cancer to other organs are usually caused by late diagnosis.

Patients with severe comorbidities had only a cumulative survival proportion of 7% through the second year, whereas lung cancer patients with mild comorbidities had a cumulative survival proportion of 20% in the third year. In line with previous research by Huang et al in 2015 which states that ashtma, COPD, TB is a coexisting disease affecting survival of lung cancer patients HR are 1.04, 1.56, and 1.14, respectively.[24] Other studies by Tammemagi et al in 2002 and Huang et al in 2015 also support the results of the study.[19] Predictive comorbidities in lung cancer have been shown to affect the survival of lung cancer patients such as diabetes, hyperlipidemia, cancer associated with smoking, chronic renal failure.[25, 26]

Delay in diagnosing cancer, unable to accept standard cancer treatments such as surgery, chemotherapy and radiation is a consequence for patients with lung cancer with severe comorbidities. This leads to lung cancer patients with late comorbidities in completing treatment that will ultimately also increase the risk of death.

The performance status is a tool that can be used to measure a patient's ability to perform daily routine activities and has been shown the best correlation with prognosis. The patient's performance status can be assessed by two scales, carnofsky and WHO scale.

Karnofsky's performance status, when used by a trained doctor, is a reliable, valid, simple, and independent predictor of survival.[27] Therefore, this study uses the karnofsky scale. The 0-100 scale is categorized into two: <70 score is a poor performance status, and the score ≥ is a good performance status.

The results of this study are in line with Supartono and Suryanto's research in 2012 that the log rank test on performance status (karnofsky scale) <70 affects 1 year of significant survival.[16] Similarly, a study by Soares et al 2007 found that patients with poor performance status were associated with lung cancer deaths with HR = 4.98 (CI 1.37-18.08).[28] This is also confirmed by Simmonsa et al. In 2014, finding performance status (ECOG / WHO) was a predictor factor for lung cancer survival with HR 1.90 (1.65-2.18).[29]

CONCLUSION

The conclusion in this study is the survival of lung cancer in Dr Wahidin Sudirohusodo is still very low. This is influenced by several factors such as patient IMT, comorbidity and performance status. For lung cancer patients to maintain nutritional intake because cancer patients have greater nutritional needs to undergo treatment, especially when patients already have comorbidities that will complicate the treatment, it is necessary to increase health promotion activities to increase knowledge about the type of lung cancer treatment to understand the mechanism, Effects, and functions. For further research, it is advisable to conduct in-depth research on the interactions of other factors that may affect the survival of lung cancer patients such as genetics, race/ethnicity, histological classification and metastatic history.

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ATTACHMENT

Table 1. Distribution of Lung Cancer Patients Based on Characteristics at Dr Wahidin Sudirohusodo Hospital Makassar 2012-2016

Characteristic	Event		Sensor		Total	
	n	%	n	%	n	%
Age group (year)						
21-28	2	50	2	50	4	100.0
29-37	4	80	1	20	5	100.0
38-46	15	71.4	6	28.6	21	100.0
47-55	37	84.1	7	15.9	44	100.0
56-64	37	84.1	7	15.9	44	100.0
65-73	15	78.9	4	21.1	19	100.0
74-82	6	100.0	0	0.0	6	100.0
83-90	1	100.0	0	0.0	1	100.0
Gender						
Male	88	81.5	20	18.5	108	100.0
Female	29	80.6	7	19.4	36	100.0
Regional characteristic						
Urban	63	76.8	19	23.2	82	100.0
Rural	54	87.1	8	12.9	62	100.0
Occupation						
Labor/fisherman/farmer	41	83.7	8	16.3	49	100.0
Private employee	5	71.4	2	28.6	7	100.0
Retired	11	78.6	3	21.4	14	100.0
Civil servant/police	15	71.4	6	28.6	21	100.0
Not working/housewife	27	90.0	3	10.0	30	100.0
Entrepreneur/self-employed	18	78.3	5	21.7	23	100.0
Smoking history						
Smoking	92	83.6	18	16.4	110	100.0
Not smoking	25	73.5	9	26.5	34	100.0
Total	**117**	**81.2**	**27**	**18.8**	**144**	**100.0**

Source: primary and secondary data, 2016

Table 2 Distribution of survival status, log rank values and HR of lung cancer patients based on independent variables in Dr. Wahidin Sudirohusodo Hospital Makassar in 2012-2016

Variable	Survival Status				Total		HR	95% CI	
	Event		Sensor					LL	UL
	n	%	n	%	n	%			
IMT									
< 18.5	103	88.0	11	40.7	108	79.2	3.163	1.802	5.551
≥ 18.5	14	12.0	16	59.3	36	20.8			
Comorbidity									
Severe	56	47.9	5	18.5	61	42.4	1.599	1.110	2.302
Mild	61	52.1	22	81.5	83	57.6			
Performance status									
Poor	82	70.1	11	40.7	93	64.6	1.987	1.335	2.960
Good	35	29.9	16	59.3	51	35.4			

Source: primary and secondary data, 2016

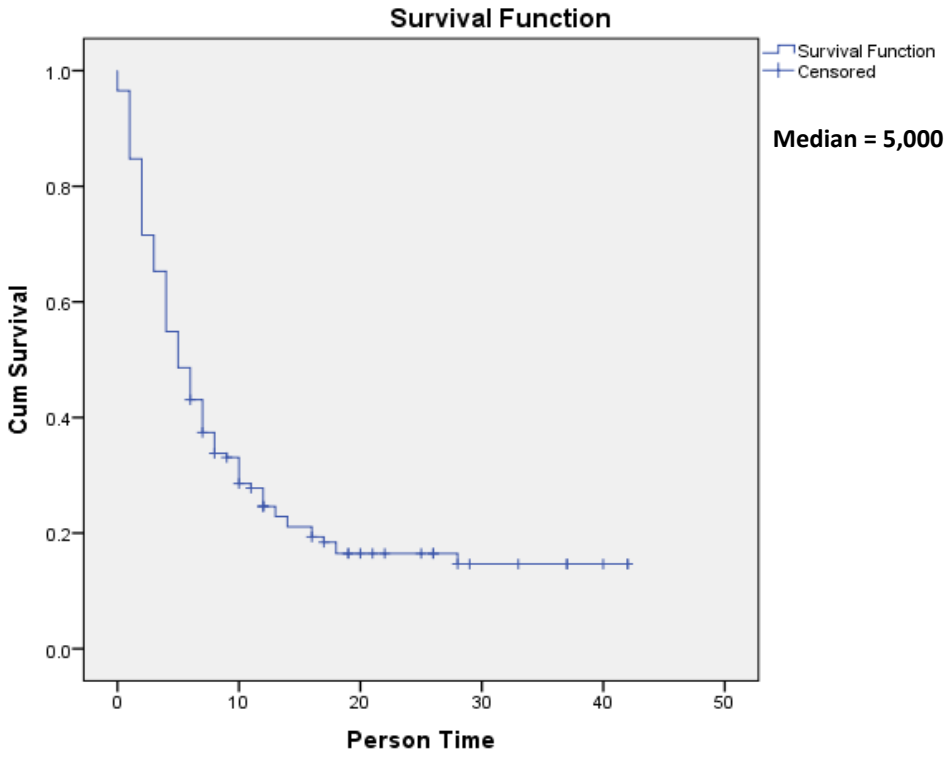

Figure 1. The survival curve of lung cancer patients in Dr. Wahidin Sudirohusodo Hospital Makassar 2012-2016

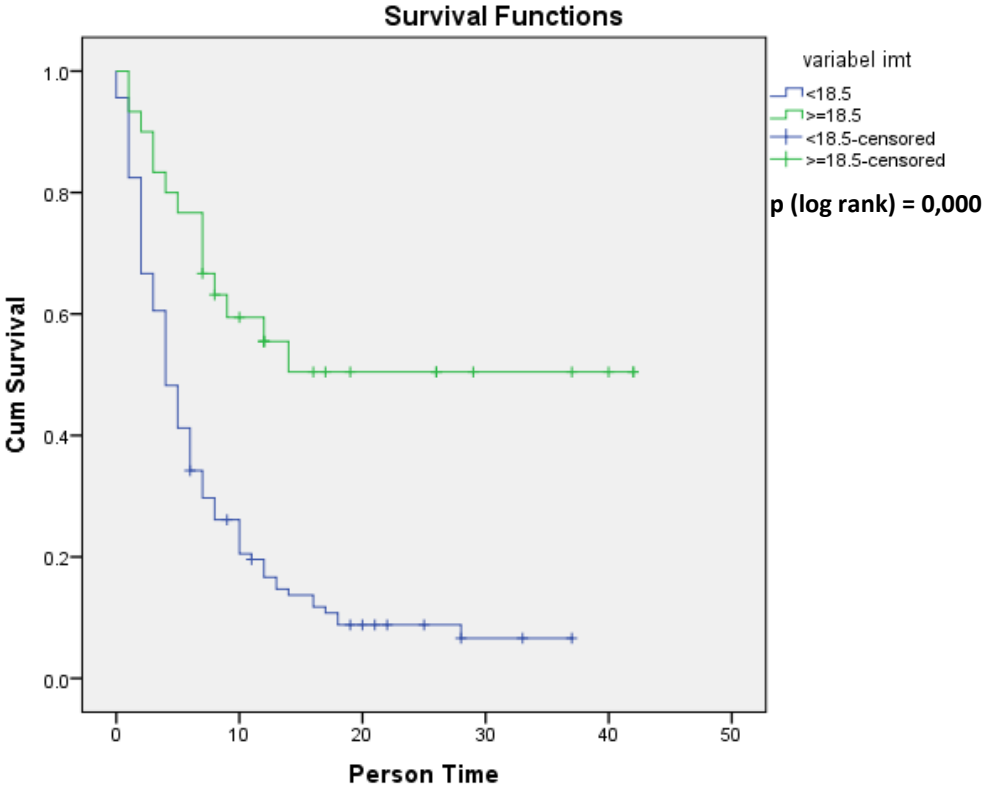

Figure 2. The survival curve of lung cancer patients based on BMI in Dr. Wahidin Sudirohusodo Hospital Makassar in 2012-2016

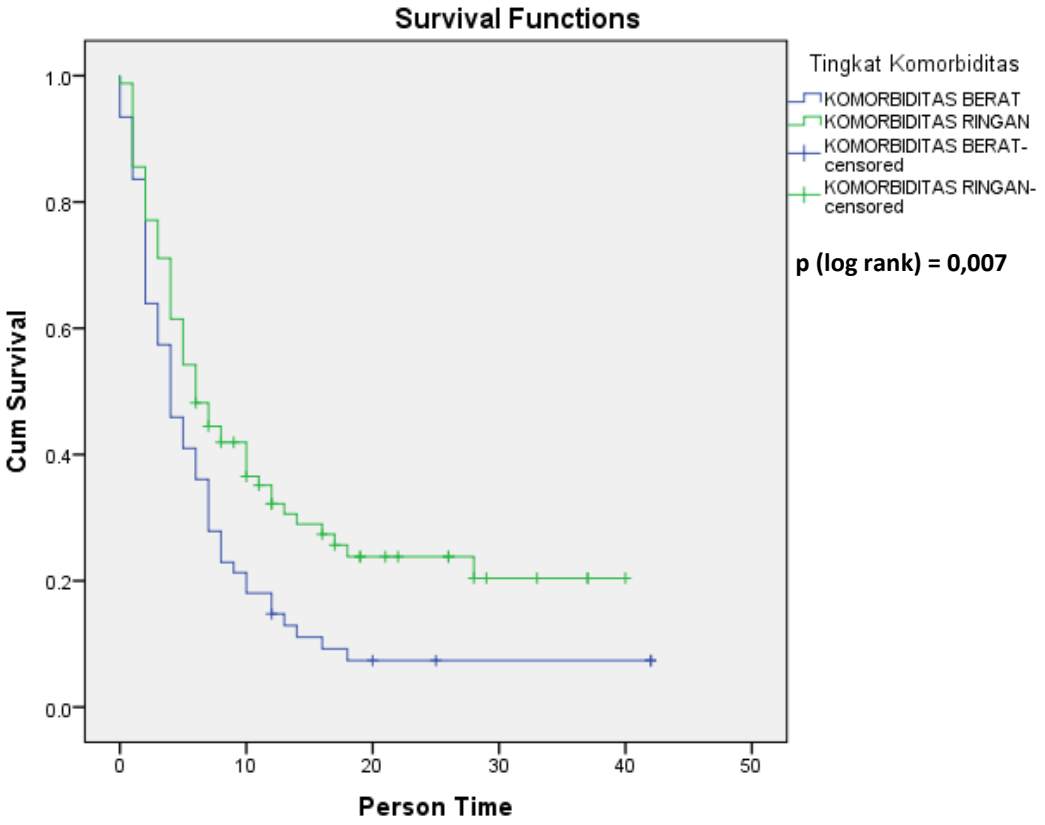

Figure 3. The survival curve of lung cancer patients based on comorbidity in Dr. Wahidin Sudirohusodo Hospital Makassar 2012-2016

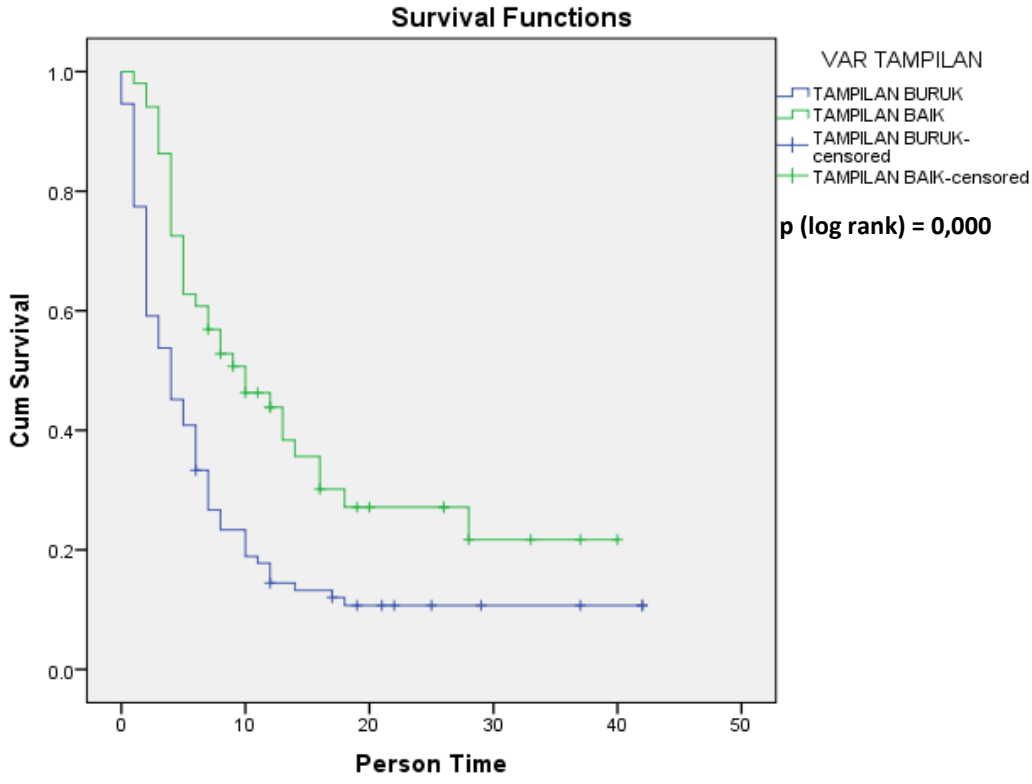

Figure 4. The survival curve of lung cancer patients is based on display status in Dr. Wahidin Sudirohusodo Hospital Makassar 2012-2016